

CLAIMS

What is claimed is:

- 5           1. A peptide comprising an amino acid sequence of the formula:

$a^1a^2a^3Ca^5a^6a^7a^8a^9a^{10}a^{11}LQSCa^{16}a^{17}a^{18}$  (SEQ ID NO: 276)

wherein:

- 10            $a^1$  is L, P, W, F, S, Y, N, R, or H;  
             $a^2$  is L, W, F, S, Y, D, or R;  
             $a^3$  is L, I, W, Y, D, or E;  
             $a^5$  is A, L, G, D, E, or K;  
             $a^6$  is A, L, F, S, N, E, K, or H;  
             $a^7$  is L, P, Y, or N;  
15            $a^8$  is A, P, M, F, G, Q, or D;  
             $a^9$  is P, M, T, G, or S;  
             $a^{10}$  is A, V, F, H, G, or S;  
             $a^{11}$  is V, L, I, F, T, N, or K;  
             $a^{16}$  is L, I, W, M, or F;  
20            $a^{17}$  is A, G, S, W, or N;  
             $a^{18}$  is F, W, or Y; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

- 25           2. The peptide according to Claim 1 wherein:

- $a^1$  is W;  
             $a^2$  is D;  
             $a^6$  is F;  
             $a^{10}$  is A;  
30            $a^{11}$  is K;  
             $a^{16}$  is F.

3. The peptide according to Claim 1 comprising the amino acid sequence of WDMCHFSAAKLQSCFPH (SEQ ID NO:273).

5

4. A composition of matter comprising at least one peptide according to Claim 1 and at least one vehicle, wherein said composition of matter is capable of inhibiting NGF activity.

10

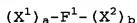
5. The composition of matter according to Claim 4 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

15

6. The peptide according to Claim 1 which is cyclic.

20 7. A dimer or multimer of the peptide according to Claim 1.

8. A composition of matter of the formula:



25 wherein:

$F^1$  is a Fc domain;

$X^1$  and  $X^2$  are each independently selected from

-  $(L^1)_c-P^1$ ;

-  $(L^1)_c-P^1-(L^2)_d-P^2$ ;

30 -  $(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3$ , and

-  $(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3-(L^4)_f-P^4$ ;

wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide according to Claim 1;

$L^1$ ,  $L^2$ ,  $L^3$ , and  $L^4$  are each independently linkers; and

- 5        a, b, c, d, e, and f are each independently 0 or 1, provided that at least one of a and b is 1; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

- 10        9. The composition of matter according to Claim 8 wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide as shown in SEQ ID NO:273.

- 15        10. The composition of matter of Claim 8 of the formula:  $F^1-X^2$ .

11. The composition of matter of Claim 8 of the formula:  $F^1-(L^1)_c-P^1$ .

20

12. The composition of matter of Claim 8 of the formula:  $F^1-(L^1)_c-P^1-(L^2)_d-P^2$ .

- 25        13. The composition of matter of Claim 8 of the formula:  $P^1-(L^1)_c-F^1-(L^2)_d-P^2$ .

14. The composition of matter of Claim 11 wherein  $F^1$  is an Fc domain or a fragment thereof.

15. The composition of matter of Claim 14 wherein F<sup>1</sup> comprises the amino acid sequence of SEQ ID NO: 60 or a fragment thereof.

5        16. The composition of matter of Claim 15 wherein L<sup>1</sup> is a peptide linker as shown in SEQ ID NO:285.

17. A polynucleotide comprising a polynucleotide sequence encoding the peptide according to Claim 1, 2,  
10    3, 6, or 7.

18. An expression vector comprising the polynucleotide of Claim 17.

15        19. A host cell comprising the expression vector of Claim 18.

20        20. The host cell according to Claim 19 wherein the cell is a prokaryotic cell.

21. The host cell according to Claim 20 wherein the cell is an *E. coli* cell.

22. The host cell according to Claim 19 wherein  
25    the cell is a eukaryotic cell.

23. A peptide comprising an amino acid sequence of the formula:

$b^1b^2b^3CWb^6b^7b^8b^9Gcb^{12}b^{13}b^{14}$  (SEQ ID NO: 274)

5 wherein:

$b^1$  is V, L, I, W, T, Y, or E;

$b^2$  is L, W, M, Q, or H;

$b^3$  is W, M, G, Q, or E;

$b^6$  is F or W;

10  $b^7$  is T or S;

$b^8$  is A, P, W, S, E, or D;

$b^9$  is A, G, Q, E, or K;

$b^{12}$  is V, I, P, D, or E;

$b^{13}$  is V, W, or Y; and

15  $b^{14}$  is P, S, or Q; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

24. The peptide according to Claim 23 wherein:

20  $b^1$  is L or I;

$b^2$  is Q or H;

$b^3$  is G or M;

$b^6$  is F or W;

$b^7$  is T or S;

25  $b^8$  is E or D;

$b^9$  is E or K;

$b^{12}$  is V or E;

$b^{13}$  is V, W, or Y;

$b^{14}$  is P, S, or Q.

30

25. The peptide according to Claim 24 comprising  
an amino sequence of IHGCVFTEEGCVWQ (SEQ ID NO: 277).

26. The peptide according to Claim 24 comprising  
5 an amino sequence of LQMCWFTEKGCEVP (SEQ ID NO: 278).

27. A composition of matter comprising at least  
one peptide according to Claim 23 and at least one  
vehicle, wherein said composition of matter is capable  
10 of inhibiting NGF activity.

28. The composition of matter according to Claim  
27 wherein said vehicle is selected from the group  
consisting of a Fc domain, polyethylene glycol, a  
15 lipid, a cholesterol group, a carbohydrate, and an  
oligosaccharide.

29. The peptide according to Claim 23 which is  
cyclic.  
20

30. A dimer or multimer of the peptide according  
to Claim 23.

31. A composition of matter having the formula:  
25  $(X^1)_a-F^1-(X^2)_b$ ,

wherein:

$F^1$  is a Fc domain;

$X^1$  and  $X^2$  are each independently selected from

$-(L^1)_c-P^1$ ;

30  $-(L^1)_c-P^1-(L^2)_d-P^2$ ;

- (L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>-(L<sup>3</sup>)<sub>e</sub>-P<sup>3</sup>; and

- (L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>-(L<sup>3</sup>)<sub>e</sub>-P<sup>3</sup>-(L<sup>4</sup>)<sub>f</sub>-P<sup>4</sup>;

wherein one or more of P<sup>1</sup>, P<sup>2</sup>, P<sup>3</sup>, and P<sup>4</sup> each

independently comprise a peptide according to Claim 23;

- 5        L<sup>1</sup>, L<sup>2</sup>, L<sup>3</sup>, and L<sup>4</sup> are each independently linkers;  
and a, b, c, d, e, and f are each independently 0 or 1,  
provided that at least one of a and b is 1; or a  
physiologically acceptable salt thereof, and wherein  
said peptide is capable of inhibiting NGF activity.

10

32. The composition of matter of Claim 31 wherein  
one or more of P<sup>1</sup>, P<sup>2</sup>, P<sup>3</sup>, and P<sup>4</sup> each independently  
comprise a peptide as shown as SEQ ID NO: 277.

15

33. The composition of matter of Claim 31 wherein  
one or more of P<sup>1</sup>, P<sup>2</sup>, P<sup>3</sup>, and P<sup>4</sup> each independently  
comprise a peptide as shown as SEQ ID NO: 278.

34. The composition of matter of Claim 31 of the  
20 formula: F<sup>1</sup>-X<sup>2</sup>.

35. The composition of matter of Claim 32 or  
Claim 33 of the formula: F<sup>1</sup>-(L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>.

- 25        36. The composition of matter of Claim 31 of the  
formula: F<sup>1</sup>-(L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>.

37. The composition of matter of Claim 31 of the  
formula: P<sup>1</sup>-(L<sup>1</sup>)<sub>c</sub>-F<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>.

30

38. The composition of matter of Claim 35, wherein F<sup>1</sup> comprises the amino acid sequence of SEQ ID NO: 60 or a fragment thereof.

5        39. A polynucleotide comprising a polynucleotide sequence encoding the peptide according to Claim 23.

40. An expression vector comprising the polynucleotide of Claim 39.

10

41. A host cell comprising the expression vector of Claim 40.

42. The host cell according to Claim 41 wherein  
15 the cell is a prokaryotic cell.

43. The host cell according to Claim 42 wherein the cell is an *E. coli* cell.

20        44. The host cell according to Claim 41 wherein the cell is a eukaryotic cell.

45. A peptide comprising an amino acid sequence of the formula: c<sup>1</sup>c<sup>2</sup>QCC<sup>5</sup>c<sup>6</sup>Sc<sup>8</sup>c<sup>9</sup>GCC<sup>12</sup>c<sup>13</sup>c<sup>14</sup>c<sup>15</sup>c<sup>16</sup>

25        wherein:

c<sup>1</sup> is V, I, T, Y, N, or K;

c<sup>2</sup> is L, M, or F;

c<sup>5</sup> is S, Q, or E;

c<sup>6</sup> is L, F, W, or Y;

30        c<sup>8</sup> is W, M, T, G, S, or N;

c<sup>9</sup> is A, V, G, S, or E;



c<sup>12</sup> is L, P, G, D, or E;

c<sup>13</sup> is K, I, L, Y, or Q;

c<sup>14</sup> is A, S, P, V, M, or Q;

c<sup>15</sup> is L or absent; and

- 5       c<sup>16</sup> is E or absent; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

46. The peptide according to Claim 45 wherein:

10       c<sup>1</sup> is K or T;

c<sup>2</sup> is L or F;

c<sup>5</sup> is E or Q;

c<sup>6</sup> is L, F, or Y;

c<sup>8</sup> is T;

15       c<sup>9</sup> is S or A; and

c<sup>12</sup> is P or L.

47. A peptide selected from the group consisting of SEQ ID NOS: 208, 209, 224, 233, 234, 241, 246, 279, and 280, or a physiologically acceptable salt thereof, wherein said peptide is capable of inhibiting NGF activity.

20

48. A composition of matter comprising at least one peptide according to Claim 47 and at least one vehicle, wherein said composition of matter is capable of inhibiting NGF activity.

25

49. The composition of matter according to Claim 48 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a

30

lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

50. The peptide according to Claim 47 which is  
5 cyclic.

51. A dimer or multimer of the peptide according to Claim 47.

10 52. A composition of matter having the formula:  
$$(X^1)_a - F^1 - (X^2)_b$$

wherein:

$F^1$  is a vehicle;

$X^1$  and  $X^2$  are each independently selected from

- 15
- $(L^1)_c - P^1$ ;
  - $(L^1)_c - P^1 - (L^2)_d - P^2$ ;
  - $(L^1)_c - P^1 - (L^2)_d - P^2 - (L^3)_e - P^3$ ; and
  - $(L^1)_c - P^1 - (L^2)_d - P^2 - (L^3)_e - P^3 - (L^4)_f - P^4$ ;

wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each  
20 independently comprise a peptide selected from the group consisting of SEQ ID NOS: 208, 209, 224, 233, 234, 241, 246, 279, and 280;

$L^1$ ,  $L^2$ ,  $L^3$ , and  $L^4$  are each independently linkers;  
and a, b, c, d, e, and f are each independently 0 or 1,  
25 provided that at least one of a and b is 1; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

53. The composition of matter of Claim 52 of the  
30 formula:  $F^1 - X^2$ .

54. The composition of matter of Claim 52 of the formula:  $F^1-(L^1)_c-P^1$ .

55. The composition of matter of Claim 52 of the  
5 formula:  $F^1-(L^1)_c-P^1-(L^2)_d-P^2$ .

56. The composition of matter of Claim 52 of the formula:  $P^1-(L^1)_c-F^1-(L^2)_d-P^2$ .

10 57. The composition of matter of Claim 54, wherein  $F^1$  is an Fc domain or a fragment thereof.

58. The composition of matter of Claim 57 wherein  $F^1$  comprises the amino acid sequence of SEQ ID NO: 60  
15 or a fragment thereof.

59. A polynucleotide comprising a polynucleotide sequence encoding the peptide according to Claim 45.

20 60. An expression vector comprising the polynucleotide of Claim 59.

61. A host cell comprising the expression vector of Claim 60.

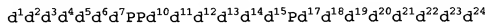
25

62. The host cell according to Claim 61 wherein the cell is a prokaryotic cell.

63. The host cell according to Claim 62 wherein  
30 the cell is an *E. coli* cell.

64. The host cell according to Claim 61 wherein the cell is a eukaryotic cell.

65. A peptide comprising an amino acid sequence  
5 of the formula:



wherein:

- d<sup>1</sup> is a W, Y, Q, or E;  
d<sup>2</sup> is a V, L, F, S, or Q;  
10 d<sup>3</sup> is a W, F, G, S, or Q;  
d<sup>4</sup> is a A, Q, D, E, or K;  
d<sup>5</sup> is a V, W, G, or R;  
d<sup>6</sup> is a M, S, Y, Q, N, E, K, or R;  
d<sup>7</sup> is a A, V, L, P, W, Q, or H;  
15 d<sup>10</sup> is a D or E;  
d<sup>11</sup> is a V or I;  
d<sup>12</sup> is a V, L, F, or Y;  
d<sup>13</sup> is a V, L, G, Q, or E;  
d<sup>14</sup> is a Q, D, or E;  
20 d<sup>15</sup> is a W or C;  
d<sup>17</sup> is a W, Y, or Q;  
d<sup>18</sup> is a V, T, Q, N, or K;  
d<sup>19</sup> is a A, L, or P;  
d<sup>20</sup> is a P, Q, R, or H;  
25 d<sup>21</sup> is a V, I, W, D;  
d<sup>22</sup> is a A, I, S, Q, or D;  
d<sup>23</sup> is a L or absent;  
d<sup>24</sup> is a E or absent;

or a physiologically acceptable salt thereof, and  
30 wherein said peptide is capable of inhibiting NGF activity.

66. The peptide according to Claim 65 wherein:

- 5           d<sup>1</sup> is Q or Y;  
            d<sup>2</sup> is L;  
            d<sup>3</sup> is W or D;  
            d<sup>4</sup> is D, E, or K;  
            d<sup>5</sup> is V, W, or G;  
            d<sup>6</sup> is Q, K, or R;  
            d<sup>7</sup> is W or L;  
10           d<sup>10</sup> is E or D;  
            d<sup>11</sup> is V or I;  
            d<sup>12</sup> is V, L, or F;  
            d<sup>13</sup> is V, L, or G;  
            d<sup>14</sup> is Q, D, or E;  
15           d<sup>15</sup> is W or C;  
            d<sup>17</sup> is W or Y;  
            d<sup>18</sup> is Q, K, or N;  
            d<sup>19</sup> is P, V, or L;  
            d<sup>20</sup> is P or S;  
20           d<sup>21</sup> is V;  
            d<sup>22</sup> is Q or D;  
            d<sup>23</sup> is a L or absent;  
            d<sup>24</sup> is a E or absent.

25           67. A peptide selected from the group consisting of SEQ ID NOS: 203, 228, 240, 247, and 266, inclusive, or a physiologically acceptable salt thereof, wherein said peptide is capable of inhibiting NGF activity.

30           68. A composition of matter comprising at least one peptide according to Claim 65 and at least one

vehicle, wherein said composition of matter is capable of inhibiting NGF activity.

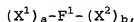
69. The composition of matter according to Claim  
5 68 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

10 70. The peptide according to Claim 65 which is cyclic.

71. A dimer or multimer of the peptide according to Claim 65.

15

72. A composition of matter having the formula:



wherein:

$F^1$  is a vehicle;

20  $X^1$  and  $X^2$  are each independently selected from

$-(L^1)_c-P^1$ ;

$-(L^1)_c-P^1-(L^2)_d-P^2$ ;

$-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3$ ; and

$-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3-(L^4)_f-P^4$ ;

25 wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide according to Claim 65;

$L^1$ ,  $L^2$ ,  $L^3$ , and  $L^4$  are each independently linkers;

and a, b, c, d, e, and f are each independently 0 or 1, provided that at least one of a and b is 1; or a

30 physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

73. The composition of matter of Claim 72 wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide selected from the group consisting of SEQ ID NOS: 203, 228, 240, 247, and 266.

74. The composition of matter of Claim 73 of the formula:  $F^1-X^2$ .

75. The composition of matter of Claim 73 of the formula:  $F^1-(L^1)_c-P^1$ .

76. The composition of matter of Claim 73 of the formula:  $F^1-(L^1)_c-P^1-(L^2)_d-P^2$ .

77. The composition of matter of Claim 73 of the formula:  $P^1-(L^1)_c-F^1-(L^2)_d-P^2$ .

78. The composition of matter of Claim 75, wherein  $F^1$  is an Fc domain or a fragment thereof.

79. The composition of matter of Claim 78 wherein  $F^1$  comprises the amino acid sequence of SEQ ID NO: 60 or a fragment thereof.

80. A polynucleotide comprising a polynucleotide sequence encoding the peptide according to Claim 65.

81. An expression vector comprising the polynucleotide of Claim 80.

82. A host cell comprising the expression vector of Claim 81.

83. The host cell according to Claim 82 wherein  
5 the cell is a prokaryotic cell.

84. The host cell according to Claim 83 wherein the cell is an *E. coli* cell.

10 85. The host cell according to Claim 82 wherein the cell is a eukaryotic cell.

86. A peptide comprising an amino acid sequence of the formula:

15 f<sup>1</sup>f<sup>2</sup>f<sup>3</sup>f<sup>4</sup>f<sup>5</sup>f<sup>6</sup>f<sup>7</sup>f<sup>8</sup>f<sup>9</sup>f<sup>10</sup>f<sup>11</sup>Lf<sup>13</sup>EQYFf<sup>18</sup>Lf<sup>20</sup>PPGf<sup>24</sup>f<sup>25</sup>f<sup>26</sup>

wherein:

- f<sup>1</sup> is A or absent;  
f<sup>2</sup> is Q or absent;  
f<sup>3</sup> is L, M, T, Q or N;  
20 f<sup>4</sup> is A, I, P, T, G, or Q;  
f<sup>5</sup> is M, G, E, or D;  
f<sup>6</sup> is W or H;  
f<sup>7</sup> is L, P, or M;  
f<sup>8</sup> is G, L, R, or S;  
25 f<sup>9</sup> is A, Q, D, or E;  
f<sup>10</sup> is L, N, or M;  
f<sup>11</sup> is P, R, or S;  
f<sup>13</sup> is L, F, or Y;  
f<sup>18</sup> is A, Q, E, or R;  
30 f<sup>20</sup> is T, M, or I;  
f<sup>24</sup> is L, I, V, or Y;



f<sup>25</sup> is a L or absent; and  
f<sup>26</sup> is a E or absent, or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

5

87. The peptide according to Claim 86 wherein:

f<sup>1</sup> is A or absent;  
f<sup>2</sup> is Q or absent;  
f<sup>3</sup> is M, Q, or N;  
10 f<sup>4</sup> is I, P, T, or G;  
f<sup>5</sup> is M, G, or D;  
f<sup>6</sup> is W or H;  
f<sup>7</sup> is L or P;  
f<sup>8</sup> is G, L, or S;  
15 f<sup>9</sup> is A, Q, or D;  
f<sup>10</sup> is L, N, or M;  
f<sup>11</sup> is P, R, or S;  
f<sup>13</sup> is L or F;  
f<sup>18</sup> is A, Q, or E;  
20 f<sup>20</sup> is T, M, or I;  
f<sup>24</sup> is L, I, or V;  
f<sup>25</sup> is a L or absent;  
f<sup>26</sup> is a E or absent.

25 88. A peptide selected from the group consisting of SEQ ID NOS: 210, 230, 232, 236, 239, and 251, inclusive, or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

30

89. A composition of matter comprising at least one peptide according to Claim 86 and at least one vehicle, and wherein said peptide is capable of inhibiting NGF activity.

5

90. The composition of matter according to Claim 89 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

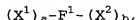
10

91. The peptide according to Claim 86 which is cyclic.

15

92. A dimer or multimer of the peptide according to Claim 86.

93. A composition of matter having the formula:



20 wherein:

$F^1$  is a vehicle;

$X^1$  and  $X^2$  are each independently selected from

$-(L^1)_c-P^1$ ;

$-(L^1)_c-P^1-(L^2)_d-P^2$ ;

25

$-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3$ ; and

$-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3-(L^4)_f-P^4$ ;

wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide according to Claim 86;

$L^1$ ,  $L^2$ ,  $L^3$ , and  $L^4$  are each independently linkers;

30

and a, b, c, d, e, and f are each independently 0 or 1, provided that at least one of a and b is 1; or a

physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

94. The composition of matter of claim 93 wherein  
5 one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide selected from the group consisting of SEQ ID NOS: 210, 230, 232, 236, 239, and 251.

95. The composition of matter of Claim 93 of the  
10 formula:  $F^1-X^2$ .

96. The composition of matter of Claim 93 of the formula:  $F^1-(L^1)_c-P^1$ .

15 97. The composition of matter of Claim 93 of the formula:  $F^1-(L^1)_c-P^1-(L^2)_d-P^2$ .

98. The composition of matter of Claim 93 of the formula:  $P^1-(L^1)_c-F^1-(L^2)_d-P^2$ .

20 99. The composition of matter of Claim 96 wherein  $F^1$  is an Fc domain or a fragment thereof.

100. The composition of matter of Claim 96 wherein  $F^1$  comprises the amino acid sequence of SEQ ID  
25 NO: 60 or a fragment thereof.

101. A polynucleotide comprising a polynucleotide sequence encoding the peptide according to Claim 86.

30 102. An expression vector comprising the polynucleotide of Claim 101.

103. A host cell comprising the expression vector of Claim 102.

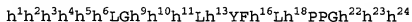
5        104. The host cell according to Claim 103 wherein the cell is a prokaryotic cell.

105. The host cell according to Claim 104 wherein the cell is an *E. coli* cell.

10

106. The host cell according to Claim 103 wherein the cell is a eukaryotic cell.

107. A peptide comprising an amino acid sequence of the formula:



wherein:

- h<sup>1</sup> is A or absent;  
h<sup>2</sup> is Q or absent;  
20    h<sup>3</sup> is V, G, P, or absent;  
h<sup>4</sup> is V, T, S, K, or absent;  
h<sup>5</sup> is S, E, Q, or D;  
h<sup>6</sup> is Q, N, K, or M;  
h<sup>9</sup> is S, G, Q, or D;  
25    h<sup>10</sup> is W, Y, or F;  
h<sup>11</sup> is A, L, or M;  
h<sup>13</sup> is Q, N, or Y;  
h<sup>16</sup> is K, H, S, or R;  
h<sup>18</sup> is A, V, L, or I;  
30    h<sup>22</sup> is S, T, or G;  
h<sup>23</sup> is L or absent;

h<sup>24</sup> is E or absent; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

- 5           108. The peptide according to Claim 107 wherein:
- h<sup>1</sup> is A or absent;
- h<sup>2</sup> is Q or absent;
- h<sup>3</sup> is P or absent;
- h<sup>4</sup> is T or absent;
- 10          h<sup>5</sup> is E or D;
- h<sup>6</sup> is Q or N;
- h<sup>9</sup> is E or D;
- h<sup>10</sup> is W or Y;
- h<sup>11</sup> is L or M;
- 15          h<sup>13</sup> is Q or N;
- h<sup>16</sup> is K or R;
- h<sup>18</sup> is V or L;
- h<sup>22</sup> is S or T;
- h<sup>23</sup> is L or absent;
- 20          h<sup>24</sup> is E or absent.

109. A peptide selected from the group consisting of SEQ ID NOS: 202, 211, 219, 221, 231, 237, and 272, inclusive, or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.
- 25

110. A composition of matter comprising at least one peptide according to Claim 107 and at least one vehicle, and wherein said peptide is capable of inhibiting NGF activity.
- 30

111. A composition of matter comprising at least one peptide selected from the group consisting of SEQ ID NOS: 202, 211, 219, 221, 231, 237, and 272, inclusive, and a vehicle, and wherein said composition of matter is capable of inhibiting NGF activity.

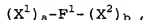
112. The composition of matter according to Claim 110 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

113. The composition of matter according to Claim 111 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

114. The peptide according to Claim 107 which is cyclic.

115. A dimer or multimer of the peptide according to Claim 107.

116. A composition of matter having the formula:



wherein:

$F^1$  is a vehicle;  
 $X^1$  and  $X^2$  are each independently selected from

- (L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>;
- (L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>;
- (L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>-(L<sup>3</sup>)<sub>e</sub>-P<sup>3</sup>; and
- (L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>-(L<sup>3</sup>)<sub>e</sub>-P<sup>3</sup>-(L<sup>4</sup>)<sub>f</sub>-P<sup>4</sup>;

- 5 wherein one or more of P<sup>1</sup>, P<sup>2</sup>, P<sup>3</sup>, and P<sup>4</sup> each independently comprise a peptide according to Claim 107;

- L<sup>1</sup>, L<sup>2</sup>, L<sup>3</sup>, and L<sup>4</sup> are each independently linkers; and a, b, c, d, e, and f are each independently 0 or 1, 10 provided that at least one of a and b is 1; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

117. The composition of matter of Claim 116 15 wherein one or more of P<sup>1</sup>, P<sup>2</sup>, P<sup>3</sup>, and P<sup>4</sup> each independently comprise a peptide selected from the group consisting of SEQ ID NOS: 202, 211, 219, 221, 231, 237, and 272.

- 20 118. The composition of matter of Claim 117 of the formula: P<sup>1</sup>-X<sup>2</sup>.

119. The composition of matter of Claim 117 of the formula: P<sup>1</sup>-(L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>. 25

120. The composition of matter of Claim 117 of the formula: P<sup>1</sup>-(L<sup>1</sup>)<sub>c</sub>-P<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>.

121. The composition of matter of Claim 117 of the formula: P<sup>1</sup>-(L<sup>1</sup>)<sub>c</sub>-F<sup>1</sup>-(L<sup>2</sup>)<sub>d</sub>-P<sup>2</sup>.

122. The composition of matter of Claim 119 wherein F<sup>1</sup> is an Fc domain or a fragment thereof.

123. The composition of matter of Claim 122  
5 wherein F<sup>1</sup> comprises the amino acid sequence of SEQ ID NO: 60 or a fragment thereof.

124. The composition of matter of Claim 123 wherein P<sup>1</sup> is a peptide of SEQ ID NO:219 and L<sup>1</sup> is a  
10 peptide of SEQ ID NO:285.

125. The composition of matter of Claim 123 wherein P<sup>1</sup> is a peptide of SEQ ID NO:219 and L<sup>1</sup> is a  
peptide of SEQ ID NO:286.

15

126. A polynucleotide comprising a polynucleotide sequence encoding the peptide according to Claim 113.

127. An expression vector comprising the  
20 polynucleotide of Claim 126.

128. A host cell comprising the expression vector of Claim 127.

25 129. The host cell according to Claim 128 wherein the cell is a prokaryotic cell.

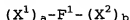
130. The host cell according to Claim 129 wherein the cell is an *E. coli* cell.

30



131. The host cell according to Claim 128 wherein the cell is a eukaryotic cell.

132. A composition of matter comprising an amino acid sequence of the formula:



wherein:

$F^1$  is an Fc domain;

$X^1$  and  $X^2$  are each independently selected from  
10  $-(L^1)_c-P^1$ ,  $-(L^1)_c-P^1-(L^2)_d-P^2$ ,  $-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3$ ,  
and  $-(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3-(L^4)_f-P^4$ ;

$L^1$ ,  $L^2$ ,  $L^3$ , and  $L^4$  are each independently linkers;

$a$ ,  $b$ ,  $c$ ,  $d$ ,  $e$ , and  $f$  are each independently 0 or  
1, provided that at least one of  $a$  and  $b$  is 1; and  
15  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  are each independently sequences  
selected from the group consisting of:

i. SEQ ID NO: 1 to SEQ ID NO: 58, inclusive;

ii. SEQ ID NO: 202 to SEQ ID NO: 280,

inclusive;

20 iii. an analog of (i) or (ii); and

iv. a derivative of (i), (ii) or (iii); or a  
physiologically acceptable salt thereof, and wherein  
said composition of matter is capable of inhibiting NGF  
activity.

25

133. The composition of matter of Claim 132  
comprising an amino acid sequence of the formula:



wherein:

30  $F^1$  is an Fc domain;

$L$  is a linker; and

P is selected from the group consisting of:

- i. SEQ ID NOS: 8, 10, 23, and 24;
  - ii. an analog of (i); and
  - iii. a derivative of (i) or (ii); or a
- 5 physiologically acceptable salt thereof, and wherein said composition of matter is capable of inhibiting NGF activity.

134. A method of treating or preventing a disease  
10 or disorder associated with NGF activity comprising administering, to a human or animal subject, a therapeutically effective amount of a composition of matter according to Claim 124, 125, 156, 157, 158, 159, 160, 161, 162, or 163.

15  
135. The method according to Claim 134 wherein the disease or disorder is selected from the group consisting of neurologic pain, painful diabetic neuropathy, post-herpetic neuralgia, inflammatory pain,  
20 migraine, asthma, hyperactive bladder, psoriasis and cancer.

136. The method of Claim 134 wherein the disease or disorder is pain.  
25

137. The method of Claim 134 wherein the disease or disorder is selected from the group consisting of acute pain, dental pain, pain from trauma, surgical pain, pain resulting from amputation or abscess,  
30 causalgia, demyelinating diseases, trigeminal neuralgia, cancer, chronic alcoholism, stroke, thalamic

- pain syndrome, diabetes, acquired immune deficiency syndrome ("AIDS"), toxins and chemotherapy, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general
- 5 inflammation, arthritis, rheumatic diseases, lupus, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, sunburn, carditis, dermatitis,
- 10 myositis, neuritis, collagen vascular diseases, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained
- 15 pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, post-herpetic neuralgia, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin
- 20 reactions, pruritis, vitiligo, general gastrointestinal disorders, colitis, gastric ulceration, duodenal ulcers, vasomotor or allergic rhinitis, or bronchial disorders.
- 25 138. A method for inhibiting pain or promoting analgesia comprising administering, to a human or animal subject, a therapeutically effective amount of a composition of matter according to Claim 124, 125, 156, 157, 158, 159, 160, 161, 162, or 163

139. A peptide comprising an amino acid sequence selected from the group consisting of:

- i. SEQ ID NOS: 8, 10, 23, or 24;
- ii. an analog of (i); and
- 5       iii. a physiologically acceptable salt of (i) or (ii), wherein said peptide is capable of inhibiting NGF activity.

140. A composition of matter comprising at least one peptide according to Claim 139 and at least one vehicle, wherein said composition of matter is capable of inhibiting NGF activity.

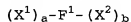
141. The composition of matter according to Claim 15 140 wherein said vehicle is selected from the group consisting of a Fc domain, polyethylene glycol, a lipid, a cholesterol group, a carbohydrate, and an oligosaccharide.

20       142. The peptide according to Claim 139 which is cyclic.

143. A dimer or multimer of the peptide according to Claim 139.

25

144. A composition of matter having the formula:



wherein:

$F^1$  is a vehicle;

30        $X^1$  and  $X^2$  are each independently selected from

- $(L^1)_c-P^1$ ;
- $(L^1)_c-P^1-(L^2)_d-P^2$ ;
- $(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3$ ; and
- $(L^1)_c-P^1-(L^2)_d-P^2-(L^3)_e-P^3-(L^4)_f-P^4$ ;

- 5 wherein one or more of  $P^1$ ,  $P^2$ ,  $P^3$ , and  $P^4$  each independently comprise a peptide according to Claim 139;

- $L^1$ ,  $L^2$ ,  $L^3$ , and  $L^4$  are each independently linkers; and a, b, c, d, e, and f are each independently 0 or 1,
- 10 provided that at least one of a and b is 1; or a physiologically acceptable salt thereof, and wherein said peptide is capable of inhibiting NGF activity.

145. The composition of matter of Claim 144 of
- 15 the formula:  $F^1-X^2$ .

146. The composition of matter of Claim 144 of the formula:  $F^1-(L^1)_c-P^1$ .

- 20 147. The composition of matter of Claim 144 of the formula:  $F^1-(L^1)_c-P^1-(L^2)_d-P^2$ .

148. The composition of matter of Claim 144 of the formula:  $F^1-(L^1)_c-F^1-(L^2)_d-P^2$ .

- 25 149. The composition of matter of Claim 145, wherein  $F^1$  is an Fc domain or a fragment thereof.

150. A polynucleotide comprising a polynucleotide
- 30 sequence encoding the peptide according to Claim 139.

151. An expression vector comprising the polynucleotide of Claim 150.

152. A host cell comprising the expression vector  
5 of Claim 151.

153. The host cell according to Claim 152 wherein the cell is a prokaryotic cell.

10 154. The host cell according to Claim 153 wherein the cell is an *E. coli* cell.

155. The host cell according to Claim 152 wherein the cell is a eukaryotic cell.

15

156. The composition of matter of Claim 58 wherein P<sup>1</sup> is a peptide of SEQ ID NO:241 and L<sup>1</sup> is a peptide of SEQ ID NO:285.

20 157. The composition of matter of Claim 58 wherein P<sup>1</sup> is a peptide of SEQ ID NO:241 and L<sup>1</sup> is a peptide of SEQ ID NO:286.

25 158. The composition of matter of Claim 96 wherein P<sup>1</sup> is a peptide of SEQ ID NO:251 and L<sup>1</sup> is a peptide of SEQ ID NO:285.

30 159. The composition of matter of Claim 96 wherein P<sup>1</sup> is a peptide of SEQ ID NO:251 and L<sup>1</sup> is a peptide of SEQ ID NO:286.

160. The composition of matter of Claim 54 wherein P is the peptide shown in SEQ ID NO:224 and L<sup>1</sup> is the peptide linker shown in SEQ ID NO:285.

5        161. The composition of matter of Claim 54 wherein P<sup>1</sup> is a peptide of SEQ ID NO:224 and L<sup>1</sup> is a peptide of SEQ ID NO:286.

10       162. The composition of matter of Claim 96 wherein P<sup>1</sup> is the peptide shown in SEQ ID NO:239 and L<sup>1</sup> is the peptide shown in SEQ ID NO:285.

15       163. The composition of matter of Claim 96 wherein P<sup>1</sup> is a peptide of SEQ ID NO:239 and L<sup>1</sup> is a peptide of SEQ ID NO:286.